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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/938,330 | 08/22/2001 | Carl Johan Friddle | LEX-0221-USA | 9990 |

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| EXAMINER | |
|---|---|
| MOORE, WILLIAM W | |
| ART UNIT | PAPER NUMBER |
| 1652 | |

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/938,330 | FRIDDLE ET AL. | |
| | Examiner | Art Unit | |
| | William W. Moore | 1652 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *27 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *2-5 and 7-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-5 and 7-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Response to Amendment*

Applicant's response filed July 27, 2004, and amending claim 2 has been entered. It is agreed that the communication mailed February 20, 2004, was a Non-Final communication. Any ambiguity is regretted. Applicant's arguments filed July 27, 2004, are persuasive in overcoming the rejections of record of claim 2 under 35 U.S.C. §112, first paragraph, for lack of enablement as to making. The rejection of record of claim 2 under the second paragraph of 35 U.S.C. §112 for indefinite description is maintained for the reasons set forth below, as well as the rejections of record of claims 2-5 and 7-11 under 35 U.S.C. §§ 101 and 112, first paragraph, for lack of patentable utility and for lack of enablement as to use for the reasons stated below and all are made final.

### *Claim Rejections - 35 USC § 101*

35 U.S.C. § 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 2-5 and 7-11 are for reasons of record rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility.

Applicant's arguments filed July 27, 2004, traversing the rejection of record have been fully considered but are not persuasive. As previously noted, a claimed invention must posses a specific, substantial and credible *in vitro* or *in vivo* utility, but the instant application cannot identify any specific, substantial, utility known to the inventors at the time the application was filed for claimed nucleic acid molecules. First, Applicant cites *In re Brana*, (34 USPQ2d 1436 (Fed. Cir. 1995), in the Response filed July 27, 2004, for the proposition that a claimed pharmaceutical compound need not be demonstrated to be ready for human consumption in order to posses a credible utility. But the invention claimed in *Brana* was a group of compounds disclosed in the application to have anti-tumor activity and there is no disclosure in the instant specification of a specific utility for

the nucleic acids, vectors and host cells of claims 2-5 and 7-11 herein known to the inventors at the time the application was filed, thus the claims are rejected because further experimentation is required to determine whatever might be a specific, substantial and credible *in vitro* or *in vivo* utility for these claimed subject matters. A claimed invention must have a "substantial utility" that provides "a specific benefit exist[ing] in currently available form". *Brenner v. Manson*, 383 U.S. 519, 534-35, 148 USPQ 689, 695 (1966) (process yields product with no utility other than as object of scientific inquiry). The filing date of the application for patent tolls the requirement for identification of a "currently available" and "specific" utility and a failure to assert "any practical use" for a compound or to "disclose any characteristics . . . that demonstrated its utility" was fatal to establishing inventorship of a chemical compound, propylene, for which specific and substantial utility was established after an Applicant's priority date. *In re Zeigler*, 992 F. 2d 1197, 11203, 26 USPQ2d 1600, 1605 (Fed. Cir. 1993).

It is agreed that polypeptides having amino acid sequences encoded by the nucleic acid sequences of either of SEQ IDs NOs:20 and 22 of claims 2-5 and 7-11 share a significant degree of amino acid sequence homology with human metalloproteases of the prior art but specification fails to disclose any specific substrate that a protease encoded by either SEQ IDs NOs:20 and 22 might cleave, whether *in vivo* or *in vitro*. Applicant argues at page 6 of the Response filed July 27, 2004, that a closely-related polypeptide, termed the "ADAMTS-14 precursor", was later discovered and that utility for a disclosed nucleic acid sequence may be predicated on this subsequent disclosure. Only a single disclosure in the specification, a sentence at page 2, lines 2-5, relates to Applicant's arguments, "The novel human proteins (NHPs) described . . . herein share structural similarity with animal proteases and particularly zinc metalloproteases", and neither of the subsequent disclosures of Colige et al. and Kevorkian et al., cited and supplied by Applicant, indicate that a product encoded by either nucleic acid molecule

claimed herein has any specific function *in vitro* or *in vivo*. Colige et al. found, page 5765, that human ADAMTS-l4 has an "aminoprocollagen peptidase activity" they could demonstrate "*in vitro* using fibroblasts lacking ADAMTS-2 activity" and Kevorkian et al. found that the expression of ADAMTS-14 transcripts, as well as expression of transcripts encoding six other metalloproteases, was elevated in osteoarthritis in human cartilage but assigned no particular role or significance to the ADAMTS-14 transcript's expression. Applicant's allegation of specific utility is not supported by a disclosure in the specification of a "structure-function relationship" establishing that a specific function is shared by structures identified in the amino acid sequences of SEQ IDs NOs:20 and 22 herein. Even if the subsequent disclosures of others concerned products encoded by the nucleic acid molecules claimed herein, they are not evidence that the instant specification disclosed a specific utility known to the inventors at the time the application was filed and there any indication in the prior art of record that the widely divergent ADAMTS family members share any specific activity, catalytic or otherwise.

Based on the subsequent disclosure of Kevorkian et al., the Response further argues, at pages 9-11, that the sequence information embodied in either of SEQ IDs NOs:20 or 22 may have a "real world", "substantial", utility if included among other, myriad, nucleic acid sequences in arrays on "DNA chips", e.g., to detect osteoarthritis as evidenced by the commercial success of enterprises producing such DNA arrays to screen transcripts captured as cDNA for tissue-specific, or physiological state-dependent, transcription. The argument is amplified to include the application of such arrays in the drug discovery process, where the presence or absence of a transcript encoding the polypeptide of SEQ ID NO:2 might, it is alleged, at least "enhance" the utility of a DNA chip or might even "provide an exquisitely specific utility for analyzing gene expression". Yet the specification fails to show what, if any, specific utility SEQ ID NO:1 might serve in such arrays, where the function of its encoded product is unknown,

other than serve as a "background" or "control". This cannot be a specific and substantial utility where any other nucleic acid sequence having no particular coding capacity would suffice as an equivalent.

At page 10 of the Response, Applicant appears to point to either or both of two assertions in the specification that expression of a disclosed nucleic acid sequence in a cell might be associated with, at page 1, "regulating development, diabetes, obesity, infertility, modulating cellular processes, and infectious disease", or at page 12, "obesity, high blood pressure, or connective tissue disorders, infertility, etc.", but there is no evidence in the specification of association of a presence or an absence in a cell, or in a tissue, of the transcript Applicant captured as SEQ ID NO:20 with any disorder, disease, or physiological condition. These assertions cannot be considered to be a disclosure of a specific utility where the specification does not indicate that Applicants were aware of any association between the expression, or the lack of expression, of a disclosed nucleic acid of SEQ IDs NOs: 20 or 22 and a specific disorder, disease, or physiological condition at the time Applicant's priority application was filed. Indeed, the assertion at page 1 of the specification is made for proteases in general and the assertion at page 12 of the specification is made for any "NHP", i.e., "novel human protease", thus no specific assertion is made for either of the polynucleotides of SEQ IDs NOs:20 or 22. While Applicant argues at page 10 of the response that the "present situation" is not analogous to that discussed by the Supreme Court in *Brenner*, it is clear that the disclosure Applicant's specification is only an invitation to experimentation to determine whether either the presence or the absence of either of SEQ ID NO:20 or SEQ ID NO:22 has anything to do with "regulating development, diabetes, obesity, infertility, modulating cellular processes, infectious disease", "high blood pressure, or connective tissue disorders", or something else entirely. A method of use of a material for further research to determine, e.g., its specific biological role, thus identifying or confirming a

'real world" context for its use, cannot be considered to be a "substantial utility". *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). The allegations of prospective, potential, utilities in the specification cannot establish a specific utility that is substantial for the claimed polynucleotides, expression vectors and host cells comprising such vectors.

Applicant finally argues, at pages 10-11 of the Response, that application of the USPTO's Utility Guidelines to the subject matter claimed herein, resulting in a failure to issue a patent bearing the presently-rejected product claims, constitutes a disregard the Constitutional right to due process. By way of comparison, Applicant cites four U.S. patents, made of record herewith, that disclose polypeptide-encoding polynucleotides and that have exemplary claims drawn to polynucleotides. There is no alleged different standard for utility apparent where none of the U.S. Patents Applicant cites discloses a nucleic acid sequence encoding all or a portion of a metalloprotease absent disclosure of a specific utility for the metalloprotease or a nucleic acid sequence encoding same. The prosecution history of the instant application is the issue Applicant must address, but nothing in the record establishes that the specification discloses a specific utility for either a metalloprotease encoded by a polynucleotide claimed herein, or for the claimed polynucleotides, known to the inventors at the time the application was filed permitting an immediate use by the public of a disclosed nucleic acid sequence, or any use by the public of an expression vector or cell comprising a disclosed nucleic acid sequence. A method of use of a material for further research to determine, e.g., its specific biological role, thus identifying or confirming a "real world" context for its use, cannot be considered to be a "substantial utility". *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). The rejection of record is therefore sustained.

*Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-5 and 7-11 are also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Applicant does not separately argue the rejection of record at page 12 of the Response filed July 27, 2004, thus the rejection of record is sustained.

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2 is for reasons or record rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejection of record is maintained because clause (b) of the amended claim 2 still recites a relative term, "highly stringent", yet states no conditions that might permit the artisan and the public seeking to determine how to differentiate between a "high" stringency, a higher stringency, or a less high stringency. Canceling clause (b) of claim 2 would, it is noted, permit a definite description of the scope of the claim without any reference to hybridization conditions because clause (a) of the claim 2 requires that any nucleic acid of the claim encode the amino acid sequence of SEQ ID NO:20. Since the artisan can design and prepare each member of this genus of isocoding nucleic acid sequences, the structural limitation in clause (a) makes clause (b) superfluous.

*Conclusion*

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is now 571.272.0933. The examiner can normally be reached between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can now be reached at 571.272.0928. The fax phone numbers for all communications for the organization where this application or proceeding is assigned remains 703.872.9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is now 571.272.1600.

William W. Moore
October 12, 2004

PONNATHAPU ACHUTAMURTHY
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